Remarks

Claims 12-23 and 26-26 are pending. Claims 16, 17, 18, 19 and 26 are amended. Support from these amendments can be found through out the specification. These amendments involve language that has been considered or suggested by the Office. Therefore, no new issues are presented in the after-final amendments. Because no new issues are presented, the present amendments should be entered and considered and their entry and consideration are respectfully requested.

Claim Objections

Claim 18 remains objected to because the adjective "fungi" is plural, whereas the noun "cell" modified is singular. It is suggested that the claim be amended to recite "fungal" rather than "fungi" in order to overcome the objection.

Claim 18 has been amended to read "cell is a bacterial, yeast or fungal cell" as suggested by the Examiner. This amendment does not narrow the claim as it only makes the claim grammatically correct. Furthermore, this amendment was not made for patentability because the claim was clear as originally written.

New Matter Rejection

The amendment filed September 26, 2001 remains objected to under 35 U.S.C. 132 because it allegedly introduces new matter into the disclosure, for the reasons of record set forth in the office action mailed July 3, 2002.

The Office maintains that the reference to Rhode in the specification is not sufficient to overcome the new matter objection as the specification does not indicate that the Rohde publication is to be incorporated by reference. Furthermore, Enzo Biochem. Inc. v. Gen-Probe is distinguishable from the instant case. In Enzo, the deposit was made by the Applicant and was incorporated by reference in the specification (296 F3d 1316, 1326). In the instant case, the sequence at issue was not deposited by the Applicants, and

was not incorporated by reference in the specification. The sequence at issue here was disclosed in a prior art reference that was mentioned in the specification.

There is no per se requirement that material supported in the specification must be incorporated by reference. The issue is whether there is support in the original specification for that which is added. The support for alleged new matter need not be *in haec verba.* The standard for whether there is support in an application is based on whether a skilled artisan would understand that the subject matter was disclosed within the specification and whether the inventor was in possession of the claimed subject matter. There can be no doubt based on the specification that the sequence disclosed in Rohde et al. was within the possession of the Applicants, or whether the Applicants intended to have the sequence of Rohde et al. constitute part of the specification.

It is true that Applicants did not literally incorporate Rhode et al., Virology 176: 648-651, 1990 by reference. However, Applicants clearly stated in the original specification that the sequence could be found in Rhode et al. Applicants gave Rhode et al. great weight and importance in the specification by referring to it in the following ways:

> The CFDV virus is located in the vascular system of the plant (cf. J.W. Randles et al.: "Localization of coconut foliar decay virus in coconut palm", Ann. Appl. Biology 1992, 601-617). A DNA associated with the disease symptoms and the occurrence of viral particles has already been cloned, sequenced and its structure determined at an earlier point in time (cf. W. Rohde et al.: "Nucleotide sequence of a circular single-stranded DNA associated with coconut foliar decay virus", Virology 176: 648-651, 1990). CFDV is a viral phytopathogen with a genome consisting of covalently closed-circular simplex DNA. Rohde et al., Virology 176: 648-651, 1990 described a DNA molecule of CFDV with a size of 1291 nucleotides and deletion mutants thereof.

Application, page 2, lines 23-37. The specification also states,

> To generate CFDV DNA fragments according to the invention, the skilled worker resorts to well-known techniques such as, for example, suitable cleavage sites of restriction endonucleases on the CFDV DNA, or the polymerase chain reaction technique which allows, starting from a full-length CFDV DNA construct, CFDV DNA fragments of the desired length to be amplified by means of specific primers. To this end, the primers are synthesized to suit the desired CFDV fragment in a manner known per se, using the nucleotide sequence of the CFDV virus, more specifically the nucleotide sequences in the region of the 5'- or 3'-ends of the desired fragment, described by W. Rohde et al. in Virology 176: 648-651, 1990.

It is clear from these two passages that the Applicants intended for the sequence disclosed in Rohde et al. to constitute part of the teaching of the application. Furthermore, the skilled artisan would understand the Rohde et al. sequence to have been disclosed. The only failure was a formal failure to use the words "incorporate by reference."

The Office, in its refusal to enter the sequence listing, focuses on the differences of the present case with Enzo rather than on the similarities and outcome of that case. The Office appears to take the position that the result in Enzo turned on the issue of the literal incorporation by reference and deposit, rather than on the totality of the evidence supporting inclusion of the sequence in that case.

In the present case, the reference Applicants made was to a specific sequence of a molecule having a particular sequence that was easily known. In fact, the disclosure of the present application contained even more information relative to the sequence of Rhode et al. than was presented by the patentee in *Enzo*. The present Applicants refer to a specific sequence in a publication. In *Enzo*, the patentee merely pointed to a molecule, the sequence of which needed to still be determined. The sequence of SEQ ID NO:1 is inherently described and disclosed by the explicit reference to Rohde. As in the case of biological deposits, one of skill in the art reading the references to Rohde in the

specification is readily able to obtain the Rohde article. Like *Enzo,* the sequence in the present case is publicly available and the specification specifically discloses exactly where one of skill in the art can find the specific sequence. Furthermore, the Rohde sequence is unalterable as it has already been published.

The Office does not seem to dispute that Applicants intended that the molecule and/or its sequence constitute part of the specification. Nevertheless, Applicants submit herewith a Declaration of Dr. Wolfgang Rohde, the lead author of Rohde et al. and an inventor of the present invention. The Declaration, attached as Exhibit A, makes provides further evidence of Applicants intent to include in its teaching the sequence of the CFDV promoter of Rhode et al.

One of skill in the art would know that the Applicants were in possession of the claimed sequence by seeing the reference to Rohde et al. in the specification and reading the disclosure of Rohde et al. Therefore, the inclusion of the sequence disclosed in Rohde is not an addition of new matter because the sequence was already a part of the specification, as one of skill in the art would understand it, and this is the standard by which one must judge the sufficiency of the disclosure. Therefore, Applicants respectfully request withdrawal of the objection.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claim 16 remains rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite in the recitation of "variant" for the reasons of record set forth in the office action mailed July 3, 2002.

The Office states that it is still unclear how different from SEQ ID NO: 1 the DNA fragment can be to be a "variant." Claim 16 also remains rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite in the recitation of "a modified promoter which does not have an activity 20% more than or 20% less than the promoter activity of nucleotides 211-911 of SEQ ID NO: 1", for the reasons of record set forth in the office action mailed July 3, 2002. The Office also maintains that one skilled in the art would not understand the claim language to mean that the DNA fragment of claim 16

demonstrates promoter activity which is within 20% of the promoter activity of the starting fragment, as the claim does not refer to "promoter activity which is within 20% of the promoter activity of the starting fragment." The Office maintains that because the metes and bounds of the claim are unclear, it cannot be determined whether the examples disclosed within the specification meet the claim limitations, and one skilled in the art could not determine whether a particular molecule would fall within the claims.

The term "variant" is commonly used and understood in this art. Furthermore, the scope of variability is clearly constrained by the requirement that the variant must have a promoter activity which is up to 20% higher or lower than that of the starting fragment as noted at page 5, lines 16-24. The Office has indicated that only certain fragments meet the claim limitations. This is certainly true; however, it not relevant to the issue of clarity under section 112, second paragraph. The determination of clarity and definiteness for purposes of this section turns on whether one of skill in the art would understand the scope and content of the claim. In the present instance, claim 16 recites a specific structure and confines its variants to a clearly defined and finite subset. Particularly, the determination of 20% variation in activity based on a known molecule using known assays for determining promoter activity define the claim in a way that the skilled scientist routinely deals with and understands. Since both the recited structure and the limits on the variants are understandable to a person in this field, the assertion by the Office that this claim is indefinite is not supported. Therefore, the claims are clear and unambiguous as written.

Claims 17-20 remain rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements, for the reasons of record set forth in the office action mailed July 3, 2002.

The Office maintains that the addition of claim 26 and the amendment of claims 17 and 19 to depend from claim 26 does not overcome the rejection. Amended claims 17 and 19 and newly added claim 26 are alleged to be indefinite for additional reasons set forth below. Claims 17 and 19 are stated to still be directed to a method of expressing a

nucleic acid by transfecting a cell with "one or more DNA fragments." The Office asserts that it is unclear how transfecting a cell with "one or more DNA fragments" would result in the expression of a nucleic acid.

Claims 17 and 19 are newly rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 17 and 19 recite the limitation "DNA fragments according to Claim 26." There is insufficient antecedent basis for "DNA fragments" in the claim 26.

Claim 26 is rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 26 recites the limitation "The composition of claim 12." There is insufficient antecedent basis for "The composition" in the claim 12.

Claim 26 is amended herein to recite "A nucleic acid which is operably linked to the DNA fragment according to claim 12." The claim no longer refers to "the composition," thus overcoming the antecedent basis issue.

Claim 17 has been amended to delete reference to "DNA fragments" and to refer to the nucleic acid of claim 26, thus overcoming the antecedent basis issue. Claim 19 has also been amended to delete reference to "DNA fragments" and to recite "transfecting a plant with the nucleic acid according to Claim 26," thus overcoming the new antecedent basis issue and the maintained clarity issue. More specifically, claims 17-19 recite a method in which a nucleic acid operably linked to a promoter ("the DNA fragment according to claim 12") is transfected into a cell, and is thereby expressed. Since the clarity issue with claim 26 is resolved, and in light of the amendments to claims 17-19, these claims overcome the present rejection, and its withdrawal is respectfully requested.

Rejections Under 35 U.S.C. § 112, first paragraph

Enablement

Claims 12, 13, 17-21 and 23 remain rejected, and claims 25-26 are newly rejected, under 35U.S.C. 112, first paragraph, because the specification, while being enabling for CFDV virus fragment of at least nucleotides comprising position 711-991 of SEQ ID NO: 1, which has promoter activity, does not reasonably provide enablement for a CFDV virus fragment that has promoter activity that only has the stem-loop structure set forth in nucleotides 962-991 of SEQ ID NO: 1, for the reasons of record set forth in the office action mailed July 3, 2002.

Claims 16 and 22 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record set forth in the office action mailed July 3, 2002.

The Office states that amendment of claims 12 and 23 to recite "nucleotides 734 to 785 set forth in SEQ ID NO: 1, and nucleotides 941 to 971 of SEQ ID NO: 1" rather than "the stem-loop structure" does not overcome the rejection. As discussed in the office action mailed July 3, 2002 at pages 6-7, the claimed promoter only requires the stem-loop structure, and does not identify the other specific region(s) necessary for promoter function. Amendment of the claims to recite the location of the nucleotides corresponding to the stem-loop structure does not provide any additional guidance with respect to the identity and location of other specific region(s) necessary for promoter function.

The Office also maintains that the specification is not enabling for any variant of SEQ ID NO: 1 or fragment thereof wherein the fragment is a modified promoter which does not have an activity 20% more than or 20% less than the promoter activity of nucleotides 211-911 of SEQ ID NO: 1. Figure 2 discloses only the stem-loop structure of

geminiviruses and CFDV, but does not disclose any particular variant of SEQ ID NO: 1, or any fragment of SEQ ID NO: 1 that has been modified. Page 5 of the specification merely asserts that the invention relates to CFDV DNA fragments having promoter function in which individual nucleotides or smaller groups of nucleotides have been subject to substitution, deletion, insertion or modification, but page 5 of the specification provides no guidance with respect to which individual nucleotides or smaller groups of nucleotides may be changed, or what type of substitutions, deletions, insertions or modifications may be made. Furthermore, the rejected claims are not directed to methods of making and testing variants of SEQ ID NO: 1 or modified fragments thereof, but to the variants and modified fragments themselves and their use as promoters. In order to enable such DNA sequences, the specification must provide sufficient guidance for one skilled in the art to be able to discriminate between operative and inoperative embodiments on the basis of their structure before they are tested or used. The disclosure of four specific fragments of CFDV that function as promoters does not provide one skilled in the art with sufficient structural information to make this determination without undue experimentation.

The Office additionally disagrees that the instant situation closely parallels the situation in *Wands*. The instant situation is distinguishable in important aspects from the facts in *Wands*. In *Wands,* the dispute over enablement centered on the predictability of producing high affinity IgM antiHBsAg antibodies for use in the claimed immunoassay methods. Here enablement centers on the predictability of variant polynucleotide sequences functioning as promoters. As discussed below with respect to the written description rejection, antibodies and promoters are structurally and functionally dissimilar molecules. Because promoters function by interacting with multiple regulatory proteins at multiple protein binding sites, and because the number and location of protein binding sites varies between different promoters, it would require undue experimentation for one skilled in the art to make and use the claimed variant promoter sequences absent guidance from the specification with respect to which nucleotides of SEQ ID NO: 1 may be changed without eliminating its promoter function. It is this type of guidance, which

is not known in the art that Applicants need to disclose in order to enable the full scope of the claimed invention.

Regarding the use of DNA fragments in transgenic plants, the Office does not dispute that techniques for plant transformation are well-known in the art and well developed. The Office maintains, however, that Applicants have not provided sufficient guidance for one skilled in the art to determine, without undue experimentation, how to use plants transformed with Applicants' specifically claimed DNA fragments. In the absence of guidance for how to use plants transformed with the claimed DNA fragments, the invention is not enabled. Applicants respectfully traverse.

Section 112, first paragraph requires that the patent specification enable those skilled in the art to make and use the full scope of the claimed invention without undue experimentation. The Office is unjustified in imposing a requirement that the "the specification must provide sufficient guidance for one skilled in the art to be able to discriminate between operative and inoperative embodiments on the basis of their structure before they are tested or used" (emphasis added). This is essentially the imposition of a "no experimentation" rule, rather than the no "undue experimentation" rule elucidate by the case law. Since this is the standard that the Office appears to be applying in the present case, the rejection is clearly improper. In any case, the specification is fully enabling for each of the claims because one of skill in the art would understand how to make and use the full scope of the claimed invention without undue experimentation. Thus, for the reasons below and those previously made of record, the pending claims should be considered enabled.

The Office has recognized that the specification is enabling for CFDV virus fragments of at least nucleotides comprising position 711-991 of SEQ. ID. NO:1. Thus, there is only unpredictability of promoter activity if modifications or deletions are made within these coordinates. This is important in at least two key regards: first with regard to the issue of enabling the scope of fragments, and second with regard to enabling the scope of variants. Because this region includes only 281 nucleotides, the number of

fragments or variants is relatively small, and these fragments and variants can be routinely produced (e.g., PCR, DNA synthesizer, etc.). The fragments and variants can be routinely screened using a variety of known assays for promoter activity.

The full scope of fragments of claims 12, 13, 16-23 and 25-26 that might potentially lack adequate promoter activity is finite and quite small. In fact, since it is clear that promoter activity resides within 711-991 of SEQ ID NO:1, only fragments which do not include these 281 nucleotides would even have the potential to effect promoter activity. Thus, contrary to the assertion of the Office, Applicants provide significant guidance as to where truncations may be made that are unlikely to affect promoter activity, i.e., anywhere outside of these coordinates. Thus, there is no issue of unpredictability of the promoter activity for the vast majority of the fragments claimed. By this teaching, applicants have also directed the skilled person to a fragment of the CFDV promoter comprising these 281 bases, which can easily be truncated within these bases, but for which routine screening would be required to determine promoter activity. There is some unpredictability for this small subset of fragments. However, the amount of screening would be relatively small due to the relatively small number of nucleotides in this region (281), and the type of work required to make and screen these fragments is routine for one ordinarily skilled in molecular biology. Thus, undue experimentation would not be required to practice the invention of claims 12, 13, 17-21, 23 and 25-26.

Regarding claims 16 and 22, the full scope of variants that might lead to changes in promoter activity outside of the recited parameters is finite and quite small. In fact, since it is clear that promoter activity resides within these coordinates, only changes to these 281 nucleotides would even have the potential to effect promoter activity. Thus, contrary to the assertion of the Office, Applicants provide significant guidance as to where modifications may be made that are unlikely to affect promoter activity, i.e., anywhere outside of these coordinates. Thus, there is no issue of unpredictability of the promoter activity for the vast majority of the variants covered by the claims. By this teaching, applicants have also directed the skilled person to a CFDV DNA fragment comprising these 281 nucleotides, which can be modified within these coordinates, but

for which routine screening would be required to determine promoter activity. There is some unpredictability for this small subset of variants. However, the amount of screening would be relatively small due to the relatively small number of nucleotides in this fragment, and the type of work required to make and screen these variants is routine for one ordinarily skilled in molecular biology. Thus, undue experimentation would not be required to practice the invention of claims 16 and 22.

Applicants have provided data demonstrating that variation across the full scope of the claims of SEQ ID NO:1 will still achieve the claimed promoter activity: deletion mutants lacking nucleotides 211 to 411 of SEQ ID NO:1 work; deletion mutants lacking nucleotides 211 to 611 of SEQ ID NO:1 work; and even deletion mutants lacking nucleotides 211 to 711 of SEQ ID NO:1 work. One of skill in the art would readily appreciate that Applicants' data indicate not only that deletion mutants will work, but also how to arrive at the specific constructs without undue experimentation. The specification also provides specific examples for creating constructs according to the invention in tobacco protoplasts and *E. coli.* (see specification at pages 11- 15). The presence of these examples is illustrative of the routine nature of making and screening variants. The fact that there are not more examples is not a sufficient basis to assert that the claims lack enablement when, as here, the scope of work that would be required to practice the non-exemplified parts of the claimed invention is constrained and well-defined.

Regarding how to use the specifically claimed fragments and variants, it is already accepted that a fragment comprising nucleotides 771-991 can be used. Based on the reasoning laid out above, undue experimentation would not be required to make and test the promoter activity of the relatively small subset of fragments or variants that might be expected to have unpredictable activity. Further, the Office acknowledges that methods of making transgenic plants with the claimed fragments are routine. Thus, it could not require undue experimentation to make and use the transgenic plants that contain the claimed CFDV DNA promoter fragments and variants.

The present case is more analogous to In re Wands than the Office asserts. This

is because the scope of fragments and variants that even might be expected to have significantly altered promoter activity is such a small subset of the claimed fragments and variants. Also, because the subset is so well defined, i.e., by sequence, there is plenty of guidance as to where one can make changes without needing to do any experimentation and where the changes may require some routine screening. Thus, even though there may be a significant amount of work required to make and screen the variant in fragments in the small subset that might be considered unpredictable, this is analogous to the type and amount of experimentation considered routine by the Wands court.

The 20% limitation of claim 16 adds a significant defining characteristic to the claim. It should be noted that the 20% variability in promoter activity is primarily relevant only to changes made in the 711-991 fragment. This is because any changes made outside of those coordinates would not be expected to have any significant variation in promoter activity. Thus, Applicants have provided two specific types of guidance for making modifications to the CFDV promoter. First, Applicants specify both the nucleotides where changes can be made without significant concern about changes in activity and the nucleotides where changes can be made with some routine screening expected to confirm promoter activity. Second, Applicants provide the 20% range to further define the changes in the nucleotides (711-991) where some variation may be expected. Thus, not only is the scope of variants with potential activity changes relatively small, the scope of what is actually covered by the claim is even smaller due to the requirement for less than 20% variability. Since the work required to determine what fragments and variants fall within both parameters (i.e. sequence coordinates and % activity against a standard) is routine in nature, and of about the same amount as would have been involved in the facts of Wands, the invention does not require undue experimentation.

Contrary to the position of the PTO, the specification provides ample guidance and working examples allowing one of skill in the art to make and use the full scope of the claims. Therefore, withdrawal of the rejections and allowance of the claims is respectfully requested.

Written Description

Claims 16 and 22 remain rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed July 3, 2002.

The Office states that while Applicants have described four specific fragments of CFDV that exhibit promoter function, Applicants have not described any variant of SEQ ID NO:1 that has promoter function, and Applicants have not described any fragment of SEQ ID NO:1 that has been modified and which does not have 20% more than or 20% less than the promoter activity of nucleotides 211-911 of changed without eliminating promoter function, and Applicants have not described what type of modifications can be made to fragments of SEQ ID NO:1 such that the fragments would exhibit the require level of promoter activity.

Regarding Applicants' argument that the written description requirement does not absolutely require disclosure of the structure of biological molecules, the Office states that Applicants fail to specifically explain why the description of four specific fragments of CFDV that exhibit promoter function is sufficient to support the description of a broad genus of promoter sequences that encompasses any variant of SEQ ID NO: 1 and every fragment thereof that is a modified promoter which does not have 20% more than or 20% less than the promoter activity of nucleotides 211-911 of SEQ ID NO: 1.

The Office also disagrees with the argument that the application of the Written Description Guidelines to antibodies is very similar to the technology at issue here. Antibodies and promoters are structurally and functionally dissimilar molecules. The Office describes antibodies as multimeric polypeptides that function by binding a specific antigen at an antigen-binding site, the location of which is common to all antibodies. The Office describes promoters as polynucleotides that function by interacting with multiple

regulatory proteins at multiple protein binding sites, many of which vary in composition and location between different promoters. The Office concludes that because antibodies and promoters are structurally and functionally dissimilar molecules, the application of the Written Description Guidelines to antibodies and promoters is different. Applicants respectfully traverse.

Applicants have described what types of modifications can be made to fragments of SEQ ID NO:1 such that the fragments would be expected to exhibit the required level of promoter activity, e.g., within 20% of the starting fragment. Particularly, Applicants have disclosed the location of the vast majority of such modifications: anything outside of 711-991 of SEQ ID NO:1. Furthermore, Applicants have disclosed the nature of modification that can be made – nucleotide insertions, deletions or substitutions of a single nucleotide or small groups of nucleotides. The specification discloses the same types of modifications within the 711-991 region, the only difference being that the skilled person would recognize that routine screening of such modified fragments would be desired. In no case, however, is there any basis to believe that the skilled person would not know the nature of the modifications disclosed.

Applicants note that the claims are shown to encompass only a finite and relatively small number of variants that might be expected to vary significantly in promoter activity. Since the scope of variants for which there is any issue that they might fall outside of the 20% range is small compared to the number of fragments which would be expected to fall within that range, the level of exemplification is sufficient. Due to the routine nature of making and screening this small subset of fragments and variants, a skilled person would view applicants as being in possession of the fragments and variants defined by the language of the specification and claims. The exemplification of 4 fragments should not be viewed as insufficient given the fact that only a relatively small number of variants might exhibit variability in promoter activity. The skilled person would be readily able to envision what is encompassed by any of the covered modifications (although there may be many). Since all that would be required to use the

variants would be viewed as routine, the person of skill would accept Applicants possession of the claimed fragments and variants based on what is taught in the application.

Applicants make note of the fact that the present CFDV promoter activity resides in a 281 nucleotide region defined by coordinates 711-991. Thus, the generic assertion that promoters are "polynucleotides that function by interacting with multiple regulatory proteins at multiple protein binding sites, many of which vary in composition and location between different promoters" is not specifically applicable to the present claims. A more accurate statement of the present facts is that CFDV promoter activity resides in a small region of SEQ ID NO:1 which has been explicitly identified by Applicants as a region sufficient for promoter activity. The issues or concern that might be relevant to promoters, in general, are not relevant here because of the teaching of the application. For the present promoter, in light of what is taught by Applicants about the promoter, the similarities with the antibodies are notable and are relevant to the application of the Written Description Guidelines to the present claims. Thus, the Guideline's analysis and conclusions for antibodies are applicable to the specific facts of the presently claimed promoter fragments and variants. Under this analysis, combined the examples and teaching of the application convey possession to the fragments and variants of the claimed invention. Thus withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. § 102

The Office maintains the rejection of Claim 16 as allegedly being anticipated by Rhode. The Office notes that while claim 23 was amended to recite that the DNA fragment does not comprise the translation start for open reading frame ORF2 as set forth as nucleotides 1215 to 1217 of SEQ ID NO:1, amended claim 16 makes no reference to the translation start site for ORF 1 and thus remains rejected.

Claim 16 has been amended herein to refer to the translation start site for ORF 1. Applicants believe this overcomes the rejection over Rohde. Reconsideration of the claims is respectfully requested.

Double Patenting

Claims 11-26 are rejected under the judicially crated doctrine of obviousness type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,303,345. The Office acknowledges that Applicants will submit a Terminal Disclaimer as appropriate when the application is in condition for allowance.

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

Payment in the amount of $930.00 is to be charged to a credit card and such payment is authorized by the signed, enclosed document entitled: Credit Card Payment Form PTO-

2038. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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I hereby certify that this correspondence or anything indicated as attached or enclosed is being deposited with the United States Postal Service as first class mail in an envelope addressed to Mail Stop: AF, Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450 on the date shown below.

Gwendolyn D. Spratt — 9-26-03

Gwendolyn D. Spratt — Date